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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,652	08/07/2001	Ronald A. Laskey	620-161	9664

7590 06/16/2004
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EXAMINER

NICKOL, GARY B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,652	LASKEY ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 88,89,101,102,104,105 and 107-111 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 88-89, 101-102, 104-105, 107-111 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Re: Laskey *et al.*

Date of priority: 05/15/1998

Response to Amendment

The Amendment filed 03-22-04 in response to the Office Action of 09-22-03 is acknowledged and has been entered.

Claims 88-89, 101-102, 104-105, 107-111 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 88-89, 101-102, 104-105, and 107-111 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Werness *et al.* Laboratory Investigation, Vol. 76, No.1, page 185A, March 1997, Abstract #1089 in further view of WO/9716731 (Dunton *et al.* 09, May 1997) for the reasons of record in the Action mailed 09-22-03.

Claims 88-89, 101-102, 104-105, and 107-111 also remain rejected under 35 U.S.C. 103(a) as being unpatentable over Todorov and Werness *et al.* (Laboratory Investigation, January 1998, Vol. 78, No. 1, pages 73-78, IDS) in further view of WO/9716731 (Dunton *et al.* 09, May 1997) for the reasons of record.

Applicant's argue (Response filed 03-22-04, page 5) that while the teachings of Werness and Todorov are concerned with the MCM2 antigen, the teachings of WO97/16731 are

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concerned with the Ki-67 antigen. Thus, applicants argue that knowledge of Ki-67 is largely irrelevant to the presently claimed invention and further disagree with any assertion of a nexus between the two antigens. This argument has been considered but is not found persuasive. To be more specific, the nexus between Ki-67 and MCM2 exist because Ki-67 was already a well-studied marker of cellular proliferation wherein both primary references (the Meeting abstract and the Laboratory Investigation article) sought it necessary to compare the immunoreaction capability of MCM2 to Ki-67 (Lab Invest, page 73, 2nd column, also Table 2). Thus, applicants' arguments that Werness and Todorov are concerned with MCM2 is only partially correct. They are concerned with MCM2, but they are also concerned with comparing the diagnostic capability of MCM2 to other well-studied markers of proliferation, like Ki-67.

Applicants further attest that the Examiner has used the present disclosure, with impermissible hindsight, to piece together an assertion of obviousness by combining references that are not concerned "with the same subject matter". This argument has been considered but is not found persuasive for the reasons set forth above. Ki-67 is one particular subject matter which is taught by all of the references.

Applicants further argue (page 6-7,10) that the Examiner's comments regarding the screening of a population of individuals is misplaced and not anticipated by the reference. Applicants propose that performing an experiment on multiple known tumors and known normal tissues would not be considered "screening of a population". Applicants have further provided a definition of screening. This argument has been considered but is not found persuasive. The dependent claims drawn to screening a population of individuals (Claims 105, 109-11) are dependent from the broadly claimed invention of a method of determining the presence or

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absence of dysplastic or neoplastic cells in a test sample containing cells from an individual comprising detecting MCM2 wherein Table 1 (Lab Invest, page 74) is clearly a screening of a population of samples from individuals. The claims do not require risk assessment and/or blindly assessing a particular population of individuals. Thus, the claimed population broadly includes screening those with tumors and those without tumors for the presence or absence of MCM2. Furthermore, assuming arguendo, that the reference does not clearly anticipate screening a population of individuals; the reference clearly suggests the possibility of using MCM2 immunoreactivity as a marker for cell proliferation for diagnostic or prognostic purposes (page 76). In this particular case, the authors have demonstrated the clinical utility of detecting MCM2 by observing its presence in 97% of the studied tumors compared to 27% of the corresponding normal tissues. Since one of the major objectives for successfully treating a cancer is diagnosing the cancer before it has metastasized, the screening of a population of individuals for MCM2 would be obvious to one of ordinary skill in the field of clinical oncology.

Applicants further argue (page 11) that there is nothing in Werness or Todorov providing any “positional information” for MCM2 expression. Applicants further argue that it would not have been obvious from either of these references that MCM2 is expressed at the surface of any tumors. This argument has been considered but is not found persuasive. With regards to positional information, it is not readily clear what applicants are referring to. The claims only recite detecting changes in the amount or pattern “whereby an increase in said amount and/or a difference in said pattern compared to normal” is assayed. Also, there is nothing in the claims regarding “expression at the surface” or “surface epithelial layers”. Hence, arguments that rely

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on a particular distinguishing feature are not persuasive when those features are not recited in the claims.

The remainder of applicants arguments have been carefully considered as well but mostly appear to argue against the references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which made up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In *re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In *re Keller* 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In *re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

June 11, 2004


GARY NICKOL
PRIMARY EXAMINER